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EXAMINER

FREDMAN, JEFFREY NORMAN

ART UNIT

PAPER NUMBER

1655

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/618,178

Applicant(s)

Lincoln et al

Examiner

Jeffrey Fredman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Dec 13, 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 51-54 and 56-74 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 51-54 and 56-74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
- 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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## **DETAILED ACTION**

### ***Priority***

1. Applicant's claim of priority back to application 08/173,173, 07/775,786 and 07/664,837 is noted. The examiner was unable to determine whether these applications provide support for the entirety of the current claims and therefore the claims are given the effective date of the immediate parent 09/088,820, which provides express support (except for claim 50, as detailed below).

### ***Claim Objections***

2. Claims 51, 52, 56, 58, 60 and 62-68 objected to because of the following informalities: The claim amendments in the response filed December 13, 2001 were not entered because no clean copy of the claims, and no marked up version of the claims, was provided. While examination as indicated below has proceeded as if the amendments were entered as requested, currently all of these claims are, in fact, indefinite as dependent from cancelled claims. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

3. The rejection of Claim 50 under 35 U.S.C. 112, first paragraph, is moot in view of the cancellation of the claim.

4. The rejection of claims 48-68 under 35 U.S.C. 112, second paragraph, are withdrawn in view of the cancellation and amendment of these claims.

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***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 50-54 and 69-74 are rejected under 35 U.S.C. 102(a) as being anticipated by Kimpton et al (PCR Meth. Appl. (August 1993) 3:13-22).

Kimpton teaches a method of determining the genotype at a locus within genetic material obtained by PCR amplification (page 14) comprising:

a) assembling reaction value data points for the samples, each reaction-value data point corresponding to a respective one of the samples and including at least one reaction value (here the data points represented by each of the separate peaks in figure 1 represents a different sample and are assembled in figure 2) (see pages 14-16),

b) determining an initial conditional probability for each reaction value data point for each genotype (here, the data was initially analyzed by analyzing the bands, to establish a conditional probability for reaction value (see page 15, subheading "statistical calculations and figure 1),

c) computing a conditional probability of each genotype for each reaction value data point (here, the calculation of band sizing determined the allele to which the sample belonged, thereby determining a genotype, since a genotype is composed of particular alleles at particular positions, see page 16, columns 2 and 3 and page 17, table 2)

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d) determining the genotype and confidence score for each reaction value data point, thus determining the genotype and confidence score at the genetic locus for each sample (here, table 2 on page 17 provides for each reaction point the genotype and a standard deviation based on the data obtained from step d) (page 16 and page 17).

Kimpton expressly teaches reacting the material at multiple loci (page 14, table 1). On page 17, Kimpton expressly considers multiple alleles in the probability distributions, particularly in table 2 which expressly notes that the method is applicable to any number of alleles. Kimpton expressly teaches the use of multiple data points derived from multiple runs of the automated apparatus including multiple data sets in the exemplified method and apparatus (page 16, especially figure 2). Kimpton expressly teaches that the locus may be dinucleotide or tetranucleotide repeats (page 13). Kimpton expressly selected the loci for their discrimination ability and teaches that several different loci may be analyzed (page 16, column 1).

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

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the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 50-54 and 60-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton in view of Clark et al (Mol. Biol. Evol. (March 1990) 7(2):111-122).

Kimpton teaches the methods of claims 50-54 and 69-74 as discussed above. Kimpton does not teach modification of the data to iteratively improve the assay.

Clark teaches a method of resolving ambiguities by performing an iterative cascade of improvements on the data points (abstract and pages 111-113). Clark also applies the method to restriction site polymorphisms.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the iterative screening and improvement methods of Clark with the probability method of Kimpton since Clark states "Details of the algorithm for extracting allelic sequences are presented here, along with some population genetic considerations that influence the likelihood of success of the method. The algorithm also applies to the problem of inferring haplotype frequencies of closely linked restriction site polymorphisms (abstract)". An ordinary practitioner would have been motivated to apply the conceptual idea of iterative data processing of Clark in the genotyping method of Kimpton in order to extract the as close to the entirety of the allelic sequences as possible. Further, an ordinary practitioner would have

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recognized that the method could be performed using any length marker, including single nucleotide polymorphisms such as the restriction site polymorphisms expressly discussed and motivated by Clark.

9. Claims 50-54 and 56-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton in view of Clark and further in view of Goelet et al (WO 92/15712).

Kimpton in view of Clark teaches the methods of claims 48-55 and 60-69 as discussed above. Kimpton in view of Clark does not teach genetic bit analysis, which includes allele specific amplification.

Goelet teaches genetic bit analysis methods, including allele specific amplification methods (see entire document, especially pages 10-13).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Kimpton in view of Clark with the use of genetic bit analysis or allele specific amplification to develop the data since Goelet states "The current invention provides a method that can be used to diagnose or characterize nucleic acids in biological samples without recourse to gel electrophoretic size separation of the nucleic acid species. This feature renders this process easily adaptable to automation and thus will permit the analysis of large numbers of samples at relatively low cost (page 8, lines 27-33)". An ordinary practitioner would have been motivated to substitute the equivalent genetic bit analysis method for PCR in order to minimize the need for gel electrophoresis and enhance the automatability of the process as expressly motivated by Goelet in order to speed analysis and minimize costs.

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10. Claims 50-54, 56, 58 and 60-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton in view of Clark and further in view of Backman et al (U.S. Patent 5,516,663).

Kimpton in view of Clark teaches the methods of claims 50-54 and 69-74 as discussed above. Kimpton in view of Clark does not the use of ligation chain reaction.

Backman teaches a method of LCR (abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Kimpton in view of Clark with the use of LCR as taught by Backman since Backman states "One of the great strengths of amplification reactions is their ability to detect exceedingly small numbers of target molecules (column 2, lines 8-10)". An ordinary practitioner would have been motivated to substitute LCR for the equivalent amplification method of PCR for the express motivation that LCR can detect small numbers of target molecules and because LCR is a known equivalent amplification assay to the PCR used by Kimpton.

### ***Response to Arguments***

11. Applicant's arguments filed December 13, 2001 have been fully considered but they are not persuasive.

Applicant's arguments are difficult to determine with precision, but Applicant first appears to argue that Kimpton does not teach that the samples have been prepared under comparable conditions. This argument is unavailing as the claim incorporates no such requirement. In



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response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., comparable conditions) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant further argues that the DNA profiling method of Kimpton does not determine the genotype and confidence scores as per claim 72. This is incorrect. The rejection shows that Kimpton teaches each element of the claimed invention.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, specific motivation is provided in the rejection. In particular, the argument that the Kimpton method worked is not evidence in any sense that an ordinary practitioner would not have been motivated to improve upon it. The entire patent system involves ordinary practitioners, by the millions, improving upon older known methods.

To the extent that Applicant relies upon overcoming Kimpton to overcome the 103 rejections, because Kimpton is maintained, so are the 103 rejections.

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***Conclusion***

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman, Ph.D. whose telephone number is (703) 308-6568.

The examiner is normally in the office between the hours of 6:30 a.m. and 4:00 p.m., and telephone calls either in the morning are most likely to find the examiner in the office.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).



**Jeffrey Fredman**  
**Primary Patent Examiner**  
**Art Unit 1655**

January 17, 2002